

- (21) Application No. 20503/78 (22) Filed 18 May 1978
(31) Convention Application No. 52/067 039
(32) Filed 7 June 1977
(31) Convention Application No. 52/084 372
(32) Filed 14 July 1977 in
(33) Japan (JP)
(44) Complete Specification published 26 Nov. 1980
(51) INT CL³ A61K 31/435, 47/00
(52) Index at acceptance

A5B 180 20X 20Y 232 23Y 26Y 285 28Y 351 35Y 382 38Y
401 402 40Y 410 411 41Y 493 49Y 501 50Y 541 54Y
566 56Y 586 58Y 650 65Y J

- (72) Inventors HIROITSU KAWATA, TADAYOSHI OHMURA,
KATSUHIKO YANO, MIKIO MATSUMURA,
SABURO HIGUCHI and YOSHIKAKI SOEISHI

(54) NIFEDIPINE-CONTAINING SOLID PREPARATION
COMPOSITION

(71) We, YAMANOUCHI PHARMACEUTICAL CO. LTD., a company organised and existing under the laws of Japan, of No. 5-1 Nihonbashi-Honcho 2-chome, Chuo-ku, Tokyo, Japan, do hereby declare the invention, for which we pray that a patent be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to solid nifedipine (4 - (2' - nitrophenyl) - 2,6-dimethyl - 3,5 - dicarboxymethoxy - 1,4 - dihydropyridine) compositions.

Nifedipine is a known material which possesses coronary dilator activity and is useful for the treatment of so-called angina pectoris attack. Since it is difficult to foresee the occurrence of angina pectoris attack, the patient is sometimes forced to treat himself when the attack occurs, and hence it is particularly desired that therapeutic substances used for the treatment of angina pectoris attack should be easily administered as a matter of course and exhibit their effect quickly and certainly. However, nifedipine exhibits low bioavailability on oral administration owing to its sparing solubility and is liable to be decomposed by the action of light, and the development of satisfactory pharmaceutical preparations of nifedipine has encountered great difficulty.

Hitherto, as nifedipine preparations for oral administration, there have been known tablets, pills (U.K. Patent No. 1,173,862), and oral-release capsules (U.S. Patent No. 3,784,684). Among these preparations, the tablets and pills are reported to be least effective owing to the very slow absorbability (U.S. Patent No. 3,784,684). The oral-release capsules are prepared by dissolving nifedipine using a solubilizing agent and enclosing the solution in a colored or shading capsule and hence exhibit the effect quickly and show good bioavailability; but the forms of liquid preparation are restricted and the preparation step is very complicated as compared to that for solid preparations. Furthermore, since nifedipine is ordinarily inferior in solubility, a large amount of solubilizers or solubilization aids is required for the preparation of such preparations for oral administration; the unit doses of these preparations are therefore inevitably large and in the case of commercially available liquid preparations (oral-release capsules) the weight of one capsule reaches 615 mg. Large tablets and capsules can be made as ellipsoids or oblongs to facilitate the swallowing thereof, but even then they are difficult to swallow if they weigh over 400 mg.

The inventors have discovered that a nifedipine-containing solid composition having the same high bioavailability as the aforesaid liquid preparations, but which is of smaller bulk and more easily administered, can be obtained by compounding nifedipine with a specific substance or substances.

According to this invention, there is provided a solid pharmaceutical composition comprising (1) a mixture of nifedipine and at least one 1st(a) substance selected from polyvinyl pyrrolidone, methyl cellulose, hydroxypropyl cellulose and hydroxypropylmethyl cellulose; or (2) a mixture of nifedipine, at least one 1st(b) substance



AH